REMARKS/ARGUMENTS

Favorable reconsideration by the Examiner is respectfully requested in light of the above amendments and the accompanying remarks.

The Examiner's indication that Claims 11-14 are allowable over the prior art is noted with appreciation. These claims have been amended to address the Section 112 issues, as explained more fully below, and should now be in condition for allowance.

Briefly, Applicants have discovered that there exists a specific and selective interaction between ATIP (AT2 interacting protein) and the C-terminal end (Asn314-Ser363) of the AT2 receptor. As a result, it is evident that ATIP is an important product for modifying signaling conditions associated with abnormalities in the regulation of the AT2 receptor.

Applicants have defined nucleic acid sequences encoding ATIP in different species, for example, mice and human. The nucleic acid molecules can therefore be used as tools that are capable of regulating the action of the AT2 receptor (see page 2, lines 35-38 of the specification). As a result of this discovery, there is a need for:

i) detecting nucleic acid molecules that encode the ATIP molecule in patients; therefore, it clearly emerges from the specification that Claim 2 of the present application must be interpreted as corresponding to fragments that are able to detect nucleic acid molecules encoding ATIP in a biological sample. In this context, the term homologous refers clearly to variant alleles that may be found in different patients.

and

ii) screening tools; (see for example, page 5, line 30 to page 9 line 32 of the specification). The advantages of the present invention, including methods that are comprised of finding means of modifying the signaling, the level of expression or pharmacology of the AT2 receptor, which may have therapeutic applications. Indeed, when a pathological condition has been correlated with a transduction abnormality associated with the AT2 receptor, modification of this transduction, in particular by acting on the binding of the AT2 receptor to the AT2 interacting protein (ATIP), may then possibly compensate for the pathological disorder or at least influence it.

Thus, the nucleic acid molecules of the present invention and the complementary sequences thereof, play a crucial role for solving the problems described above.

With respect to items 4 and 8 of the Official Action, Claims 2-4 stand rejected under 35 U.S.C. § 112, first and second paragraph as being indefinite and non-enabled. Applicants respectively disagree with this assertion. However, in the interest of expediting prosecution of the application, Applicants have amended Claim 1 and Claim 2. Claim 1 is amended to remove the reference to SEQ ID NO: 5. Claim 2 has been amended to include limitations recited within Claim 3 and Claim 3 has been canceled. Support for amended Claim 2 is found in the specification at page 4. With respect to the term "isolated nucleic acid encoding a protein capable of binding to the AT2 receptor," the term includes, in the context of the specification and the invention: coding gene, i.e., DNA and transcripts i.e., RNA (see page 4 of the specification).

Additionally, it is important to remember that DNA is double-stranded and that usually only one strand is taken as a reference for defining a DNA molecule. If a primer is defined in reference to one of the strands, it is common knowledge of one of ordinary skill in the art to design the forward and reverse primers that are used to amplify each strand of DNA. As well known since Saiki et al. (1985), PCR is a cyclic process of double-stranded separation of DNA by heat denaturation, specific hybridization, or annealing short oligonucleotide primers to single-stranded DNA and synthesis by DNA polymerase (See attached FIG. 1).

With respect to items 5 and 8 of the Official Action, Claim 14 has been rejected under 35 U.S.C. § 112, first and second paragraph as being indefinite and non-enabled. Applicants respectfully disagree with the interpretation of Claim 14. At the time the invention was made, AT2 receptor was known; the Applicants using the yeast two-hybrid method and by screening a mouse foetal cDNA library unexpectedly discovered that there exists a protein having specific binding interaction with the AT2 receptor. Accordingly, it is within the expertise of one of ordinary skill in the art, being apprised of the teachings herein, to modify the two proteins of the two-hybrid system in view to detect the domains necessary for the specific binding. Additionally, random and directed

mutagenesis are techniques that were also known to persons skilled in the art at the time the invention was made.

In this regard, a signed declaration of Mr. Arthur Donny Strosberg, one of the inventors, is attached. The declaration highlights the fact that modifying the coding sequences in view to obtain mutated proteins that are to be used in the yeast-two hybrid method, as described in the present application, does not constitute undue experimentation knowing what is claimed is a screening tool.

Claim 14 has been amended to more definitively recite the invention. In particular, the expression "ATIP protein" has been replaced with "AT2 interacting protein."

With respect to items 6 and 8, Claims 11-13 have been rejected under 35 U.S.C. § 112, first and second paragraph as being indefinite and non-enabled. In response to the objection, Claims 11-13 have been amended to include the expression "C-terminal end of the AT2 receptor corresponding to cytoplasmic domain of said AT2 receptor". Support for the expression can be found in the specification at page 13, lines 19-23, and page 22, lines 5-6, and in figure 1; the attached annexes I, II, and III, which were published before the filing of the present application. From the foregoing, it is clear that the C-terminal part of the AT2 receptor corresponds to the cytoplasmic domain. In particular, figures 1 and 2 of annex I, shows that the cytoplasmic domain begins at position 314, as specified in the present application at page 22, lines 5-6.

The Office action has also objected to the use of the expression "ATIP protein." This term has been replaced with "AT2 interacting protein".

Claims 1-5 have been rejected for lack of novelty based on Bonaldo et al. and Marra et. al. Claim 1 of the present application is limited to specific fragments that are not disclosed or suggested by the cited references.

Bonaldo et al. does not disclose or suggest the sequences in question. A careful review of the sequence discussed in Bonaldo et al. shows that it was not actually available to the public until after the effective filing date of the present application. In this regard, annex IVa shows that the library entry disclosing the sequence was not created until September 6, 2000. A copy of Bonaldo et al. in its entirety is attached for

your review. Thus, the Bonaldo reference is not pertinent to the novelty of the present invention. Additionally, when the article was published, only the INFLS library was studied (see annex IVb), whereas the sequence of the present invention concerns the NIH_BMAP_MAM library (see annex IVa). Thus, the invention is novel over the cited reference.

Marra et al. is exclusively directed to a sequence having 500 bp. In contrast, the present invention is directed to fragment sequences having different amounts of base pairs. Thus, Marra et al. does not describe the same sequence as the one claimed as SEQ ID NO:5. Moreover, the Blast comparison (see Blast2 sequence results of annex V) shows that the two sequences are different. Therefore, the present invention is novel over the cited reference, and in particular, SEQ NO: 5 is not disclosed by the cited reference.

Claims 9-10 have been also rejected under 35 U.S.C. § 103 as being unpatentable over Bonaldo et al. or Marra et al. Bonaldo et al. is not pertinent for reasons discussed above.

With respect to Marra, in view of the problem solved by invention, as described above, there is no suggestion or disclosure in Marra to select different fragments other than the one described in Marra for preparing a tool to study the AT2-ATIP interaction. Indeed, the fragment described in Marra is different than the fragments of the present invention. Moreover, the fragment disclosed in Marra has no clear function. Therefore Marra does not give any motivation for using the claimed fragments recited in the present application. For example, the fragments of the invention are useful for modulating the action of the AT2 receptor, and as a screening tool). Thus, Claims 9 and 10 are patentable over the cited references.

For the reasons noted, the claims as presented clearly distinguish over the cited prior art. Reconsideration by the Examiner and withdrawal of the prior art rejection are respectfully solicited.

For the reasons noted, Applicants submit that this application is in condition for immediate allowance. Favorable reconsideration by the Examiner and formal notification to this effect are respectfully solicited.

It is not believed that extensions of time or fees for net addition of claims are required, beyond those that may otherwise be provided for in documents accompanying this paper. However, in the event that additional extensions of time are necessary to allow consideration of this paper, such extensions are hereby petitioned under 37 CFR § 1.136(a), and any fee required therefore (including fees for net addition of claims) is hereby authorized to be charged to Deposit Account No. 16-0605.

Respectfully submitted,

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Grace R. Rippy